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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,243	WANG ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *10-18,20-22 and 24-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 23* is/are rejected.

7)☒ Claim(s) *7, 9 , 19 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Applicants' election of Group I, claims 1-9, 19 and 23 with respect to SEQ D NO: 1 for prosecution in their response dated 06/27/08 is acknowledged. Because applicants' did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)) and hence the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1-30 are pending in this application and claims 1-9, 19 and 23 are now under consideration. Claims 10-18, 20-22 and 24-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/27/08.

Priority

Acknowledgment is made of applicants' claim for priority under 35 U.S.C. 119(e) to the Provisional application 60/490,984 filed on 07/30/2003. This application is a 371PCT/US04/24414 filed on 07/30/2004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 05/21/06 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the IDS statement.

Objections to Abstract

The Abstract of the disclosure is objected to because, Abstract should be on a separate sheet of paper. Correction is required. See MPEP § 608.01(b).

Specification Objections

The listing of references in the specification is not a proper information disclosure

statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Appropriate correction is required.

Claim Objections

Claim 7 is objected to, due to the following informality: Claim 7 recites "… to make the protein less immunogenic". Claim 7 as written, it is not clear "less immunogenic" as compared to what? For examination purposes, claim 7 is interpreted as being compared to non-glycosylated protein having the amino acid sequence of SEQ ID NO: 1. Clarification and appropriate correction is required.

Claim 19 is objected to, due to the following informality: Claim 19 recites "… transferring a vector…" and "…culturing a vector…". Claim 19 as written is scientifically unclear. For examination purposes, claim 19 is interpreted as being transforming the vector comprising the nucleic acid encoding the amino acid sequence of SEQ ID NO: 1 into a host cell and culturing the host cell in a suitable medium for expressing and isolating said protein. Clarification and appropriate correction is required.

Claim 23 is objected to, due to the following informality: Claim 23 depends from non-elected claim 20. Appropriate correction is required.

Claim 23 is objected to, due to the following informality: Claim 23 recites "… having reduced immunogenecity or increased half-life…". Claim 23 as written, it is not clear "… having reduced immunogenecity or increased half-life…" as compared to what? For examination purposes, claim 23 is interpreted as being compared to protein

having the amino acid sequence of SEQ ID NO: 1 that is non-complexed to the inhibitor glucosamine and polyethylene glycol (PEG). Clarification and appropriate correction is required.

Claim Rejections 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one of skilled in the relevant art that the invention(s), at the time the application was filed, had possession of the claimed invention.

Claims 3 and 4, as interpreted are directed to a genus of molecules with wide variety of structures i.e., active site inhibitors of an isolated protein having the amino acid sequence of SEQ ID NO: 1. The specification does not contain any disclosure of the structure of all active site inhibitors included in the claimed genera. Said genera encompasses a wide variety of structurally disparate molecules such as organic, inorganic, ligands, antibodies, small molecules, short peptide domains/motifs, oligosaccharides i.e., infinitely large variety of structures. Therefore, many structurally distinct molecules are encompassed within the scope of the claims.

The specification discloses a few species of inhibitor i.e., chitosan oligosaccharide with a chain length of 4 to 7 and monomer or polymer of glucosamine (page 18 of specification), which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. A sufficient written

description of a genus of active site inhibitors of an isolated protein having the amino acid sequence of SEQ ID NO: 1 may be achieved by a recitation of structural features common to members of genus, **which features constitute a substantial portion of the genus**. There is no recited structural feature of the genus in the specification, i.e., active site inhibitors of an isolated protein having the amino acid sequence of SEQ ID NO: 1. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there is no structure correlated to associated function recited in claims with regard to the members of the genus of active site inhibitors of an isolated protein having the amino acid sequence of SEQ ID NO: 1 as claimed in claims 3 and 4.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at <http://www.uspto.gov>.

Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) when given the broadest interpretation. Claim 1 is directed to an isolated protein having the amino acid sequence of SEQ ID NO: 1 and as admitted on record by the applicants on pages 6-7 of the specification, said polypeptide is the same protein isolated by Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) and designated as N,O-Diacetylmuramidase of *Chalaropsis* species. Examiner is reproducing the relevant section from page 6 of the specification.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS
In accordance with the present invention, the present inventors have now discovered that the commonly accepted amino acid sequence for Lysozyme Ch is in error, and that the actual sequence, when isolated and produced recombinantly, will have a higher activity level and will thus be far more effective in killing bacteria that recombinant proteins produced using the incorrect original sequence. The Lysozyme enzymes from the fungus of the Chalaropsis species have been the subject of numerous articles in the field, including Hash, J. Bacteriol. 93(3):1201- 1202 (1967); Hash et al., J. Biol Chem. 242(23):5580-5590 (1967); Fouche et al., J. Biol Chem. 253(19):6787-6793 (1978); and Lyne et al., J. Biol Chem. 265(12):6928- 6930 (1990). The original sequence for Lysozyme Ch, identified as the N,O-diacetylmuramidase for the Chalaropsis species, was published by Felch et al: at J. Biol Chem. 250(10):3713-3720 (1975). Still further information about the Lysozyme Ch structure was described in Rau et al., J. Biol Chem. 276(34)31994-31999 (2001). All of the foregoing articles are incorporated herein by reference.
Following the establishment of this sequence, there had been very little challenge to the accuracy of this sequence since there had been very little in the way of structural information that was available for this enzyme. However, the present inventors carried out high resolution studies of the atomic structure of Lysozyme Ch and the information in the form of atomic coordinates is provided herewith in Appendix A. Based on these high resolution studies, and the electron density data obtained therein, the present inventors have thus determined that the actual sequence for Lysozyme Ch differs in important ways than the sequence as disclosed in prior references and until now considered the accurate Lysozyme Ch sequence. The corrected sequence is shown below in comparison to the "original" incorrect sequence, and the changes from the original sequence are highlighted in bold text:

Original
TVQGFDISSY QPSVNFAGAY SAGARFVIIK ATEGTSYTNP 40

Felch et al., (*supra)* disclose the purification, and the complete amino acid sequence of N,O-Diacetylmuramidase of *Chalaropsis* species. The amino acid sequence reported by Felch et al., was established via a combination of automated and manual Edman degradation and carboxypeptidase digestion of the isolated and purified protein and said amino acid sequence has 94.2% sequence homology to SEQ ID NO: 1 as a result of sequencing error (as admitted by the applicants in the specification). Because the enzyme in the reference (Felch et al.,) is a N,O-Diacetylmuramidase of *Chalaropsis* species and isolated from the same source (*Chalaropsis* species) as in the instant application, the two enzymes are identical and that the reference enzyme isolated by Felch et al., inherently has the same amino acid sequence as that of SEQ ID NO: 1 of the instant application. Therefore the reference of by Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) anticipates claim 1. Furthermore, examiner finds support for the rejection in the following sections of M.P.E.P.

MPEP Chapter 2100-Patentability, clearly states that "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.< See also MPEP § 2112.01 with regard to inherency and product-by-process claims and MPEP § 2141.02 with regard to inherency and rejections under 35 U.S.C. 103".

Examiner has applied similar lines of argument as per **MPEP Chapter 2100-Patentability,** that applicants discovery of an inherent property of previously disclosed prior art product i. e., the enzyme in the reference (Felch et al.,) is a N,O-Diacetylmuramidase of *Chalaropsis* species and isolated from the same source (*Chalaropsis* species) as in the instant application and the correction of a previously reported sequence error does not make the applicants' invention novel and hence the instant application claim 1 is fully anticipated by the cited prior art.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) in view of Fouche et al., (J. Biol. Chem., 1978, Vol. 253 (19): 6787-6793) and Veronese et al., (U.S. Patent No.: 5, 514,572, date of patent 05/07/1996). Claims 1-6, 8 and 23 are directed to an isolated protein having the amino acid sequence of SEQ ID NO: 1, said protein is attached to i) a polyethylene glycol to make the protein less immunogenic or to increase the half-life (as in claim 2); ii) complexed with an active site inhibitor such as

a glucosamine (as in claims 3-6), iii) pharmaceutical composition comprising said polypeptide (as in claim 8) and iii) a *Chalaropsis* lysozyme having reduced imounogenicity or increased half-life (as in claim 23).

The reference of Felch et al., disclose the isolation of *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) and the structure of the said enzyme (also see 102 (b) rejection and examiner's interpretation above). The reference of Felch et al., although discloses the isolation of *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) (same as the instant invention), said reference is silent regarding (A) oligosaccharides of chitosan as well as monomer or polymer of glucosamine as inhibitors of said enzyme and (B) said protein is attached to i) a polyethylene glycol to make the protein less immunogenic or to increase the half-life (as in claim 2); ii) complexed with an active site inhibitor such as a glucosamine (as in claims 3-6), iii) pharmaceutical composition comprising said polypeptide (as in claim 8) and iii) a *Chalaropsis* lysozyme having reduced immunogenecity or increased half-life (as in claim 23).

Fouche et al., disclose oligosaccharides of chitosan and as well as free glucosamine being inhibitors of *Chalaropsis* lysozyme (Abstract section, page 6787 and entire document).

Veronese et al., disclose a method of conjugating/modification of any enzyme of interest with polyethylene glycol (PEG) to obtain adducts having valuable properties for use in the biomedical field (less immunogenic or to increase half-life, column 1, lines 20-25; pharmaceutical compositions) and as novel biocatalysts due to the presence of PEG chains of defined length at the surface and proteins conjugates of PEG and

pharmaceutical compositions. Said reference also discloses methods for preparing enzyme-PEG adducts wherein an immobilized reversible inhibitor is employed in the preparation of enzyme-PEG glycol adducts that prevents reaction of PEG with the active site of the enzyme and such enzyme preparations had improved activity against macromolecular substrates as compared to enzyme-PEG adducts without the active site inhibitor (Abstract section and entire document). Veronese et al., also teach that on one hand while the PEG adduct forms an hydration cloud around the enzyme surface that maintains activity of the enzyme against small molecules/substrates and prevents access of larger molecules such as proteolytic enzymes as well as recognition by the immune system and, on the other hand PEG-enzyme adducts prevents or diminishes activity of enzyme towards large substrates. To allow access for macromolecular substrates (proteins, nucleic acids and polysaccharides) to the active site, the PEG binding to the enzyme is carried out in heterogeneous phase, in which the enzyme is linked to an inhibitor thereof, in such a way the PEG polymer will bind enzyme areas far from the active site and its proximity, thus allowing the approach of substrate molecules and preserving the full-activity of enzymes conjugated with PEG (Columns 1-2).

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Felch et al., Fouche et al., and Veronese et al., to prepare an isolated protein having the amino acid sequence of SEQ ID NO: 1 for use in the biomedical field (less immunogenic or to increase half-life; pharmaceutical compositions) and as novel biocatalysts, said protein is attached to i) a polyethylene glycol to make the protein less immunogenic or to increase the half-life; ii) complexed

with an active site inhibitor such as a glucosamine and iii) a *Chalaropsis* lysozyme having reduced imounogenicity or increased half-life, as protein having the amino acid sequence of SEQ ID NO: 1 is *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) and acts on large substrates like chitosan oligosaccharides comprised in bacterial cell walls, potentially having anti-bacterial effects (pharmaceutical composition). The expectation of success is high, because Felch et al., disclose the isolation of *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) including the structure of the said enzyme, Fouche et al., disclose oligosaccharides of chitosan and as well as free glucosamine being inhibitors of *Chalaropsis* lysozyme and Veronese et al., teach i) a method of conjugating/modification of any enzyme of interest with polyethylene glycol (PEG) to obtain adducts having valuable properties for use in the biomedical field and as novel biocatalysts due to the presence of PEG chains of defined length at the surface reference and ii) methods for preparing enzyme-PEG adducts wherein an immobilized reversible inhibitor is employed in the preparation of enzyme-PEG glycol adducts that prevents reaction of PEG with the active site of the enzyme and such enzyme preparations had improved activity against macromolecular substrates as compared to enzyme-PEG adducts without the active site inhibitor. Therefore, claims 1-6, 8 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) in view of Fouche et al., (J. Biol. Chem., 1978, Vol. 253 (19): 6787-6793) and Veronese et al., (U.S. Patent No.: 5, 514,572, date of patent 05/07/1996).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) in view of Fouche et al., (J. Biol. Chem., 1978, Vol. 253 (19): 6787-6793) and Veronese et al., (U.S. Patent No.: 5, 514,572, date of patent 05/07/1996) as applied to claims 1-6, 8 and 23 above, and further in view of Bailon PS., (U.S. Patent No.: 6,583,272, date of patent 06/24/2003) and Nakamura et al., (J. Biol. Chem., 1993, Vol. 268 (17): 12706-12712, in IDS). The references of Felch et al., Fouche et al., and Veronese et al., are silent regarding glycosylation and hyperglycosylation to make a protein less immunogenic (as in claim 7). Bailon PS., teach the modification of a pharmaceutically important protein erythropoietin, modified by the addition 1 to 6 glycosylation sites or rearrangement of at least one glycosylation site, said hyperglycosylated protein having increased half-life and increased clinical activity (i.e., less immunogenic) and said reference also discloses pharmaceutical compositions comprising said hyperglycosylated proteins.

Nakamura et al., also teach production of hyperglycosylated lysozyme protein in yeasts that was more stable than non-glycosylated lysozyme and retaining the enzyme activity (Abstract and Introduction section, page 12706) and it is also well known in the art that proteins produced in the yeast expression systems have increased glycosylation (hypermannosylated) that renders the expressed proteins less immunogenic.

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the teachings of Felch et al., Fouche et al., Veronese et al., Bailon PS., and Nakamura et al., to prepare an isolated protein having the amino acid sequence of SEQ ID NO: 1 for use in the biomedical field (less immunogenic or to increase half-life;

pharmaceutical compositions) and as novel biocatalysts, said protein is attached to i) a polyethylene glycol to make the protein less immunogenic or to increase the half-life; ii) complexed with an active site inhibitor such as a glucosamine and iii) a *Chalaropsis* lysozyme having reduced imounogenicity or increased half-life, as protein having the amino acid sequence of SEQ ID NO: 1 is *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) and acts on large substrates like chitosan oligosaccharides comprised in bacterial cell walls, potentially having anti-bacterial effects (pharmaceutical composition). The expectation of success is high, because Felch et al., disclose the isolation of *Chalaropsis* species Lysozyme (N,O-Diacetylmuramidase) including the structure of the said enzyme, Fouche et al., disclose oligosaccharides of chitosan and as well as free glucosamine being inhibitors of *Chalaropsis* lysozyme and Veronese et al., teach i) a method of conjugating/modification of any enzyme of interest with polyethylene glycol (PEG) to obtain adducts having valuable properties for use in the biomedical field and as novel biocatalysts due to the presence of PEG chains of defined length at the surface reference and ii) methods for preparing enzyme-PEG adducts wherein an immobilized reversible inhibitor is employed in the preparation of enzyme-PEG glycol adducts that prevents reaction of PEG with the active site of the enzyme and such enzyme preparations had improved activity against macromolecular substrates as compared to enzyme-PEG adducts without the active site inhibitor and Bailon PS., and Nakamura et al., teach hyperglycosylation of proteins for the reduction of immunogenicity and increased stability. Therefore, claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Felch et al., (J. Biol. Chem., 1975, Vol. 250

(10): 3713-3720, in IDS) in view of Fouche et al., (J. Biol. Chem., 1978, Vol. 253 (19): 6787-6793) and Veronese et al., (U.S. Patent No.: 5, 514,572, date of patent 05/07/1996) as applied to claims 1-6, 8 and 23 above, and further in view of Bailon PS., (U.S. Patent No.: 6,583,272, date of patent 06/24/2003) and Nakamura et al., (J. Biol. Chem., 1993, Vol. 268 (17): 12706-12712, in IDS).

Therefore, the above references render Claims 1-8 and 23 *prima facie* obvious to one of ordinary skill in the art.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

1. Claims 7, 19 and 23 are objected to, due to various informalities.

2. Claims 9 and 19 are objected to as they depend from rejected base claim 1.

3. Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one of skilled in the relevant art that the invention(s), at the time the application was filed, had possession of the claimed invention.

4. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) when given the broadest interpretation.

5. Claims 1-8 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) and in view of Fouche et al., (J. Biol. Chem., 1978, Vol. 253 (19): 6787-6793) and

Veronese et al., (U.S. Patent No.: 5, 514,572, date of patent 05/07/1996) and further in view of Bailon PS., (U.S. Patent No.: 6,583,272, date of patent 06/24/2003) and Nakamura et al., (J. Biol. Chem., 1993, Vol. 268 (17): 12706-12712, in IDS).

For the record examiner has not rejected claims 9 and 19 under 103 (a) obviousness rejection, said claims are drawn to an isolated nucleic acid encoding the protein of SEQ ID NO: 1 (as in claim 9) and a method of making said protein (as in claim 19) in the light of court ruling In re Deuel, 34 USPQ2d 1210 (Fed. Cir. 1995); "Existence of general method of isolating cDNA or DNA molecules is essentially irrelevant to question of whether specific molecules themselves would have been obvious, in absence of other prior art that suggests claimed DNAs, nor does fact that general process can be conceived in advance for preparing undefined compound mean that claimed specific compound was precisely envisioned and therefore obvious; Board of Patent Appeals and Interferences thus erred by rejecting claims for isolated and purified DNA and cDNA molecules encoding heparin-binding growth factors based upon alleged obviousness of method of making molecules, since applied references do not teach or suggest claimed cDNA molecules."

The amino acid sequence of *Chalaropsis* species Lysozyme disclosed by Felch et al., (J. Biol. Chem., 1975, Vol. 250 (10): 3713-3720, in IDS) contains sequencing

errors and therefore a skilled artisan would not be able to utilize the amino acid sequence information of Felch et al., (*supra*) to isolate the correct encoding cDNA.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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